REMARKS

Claims 37-65 were pending in the application. Claims 57-60, 63 and 64 are canceled and new claims 66-72 are added. Upon entry of this amendment, **claims 37-56, 61, 62 and 65-72 will be pending**.

Claims 37 and 39 are amended herein to clarify that the antigen is a "peptide" antigen, support for which can be found, for example, on page 15, lines 4-14 and on page 22, line 29 to page 23, line 15 of the specification. Claims 37, 38, 41, 45 and 49 are amended to specify that the human β_2-microglobulin molecule (hβ_2m S55V) has the amino acid sequence set forth as SEQ ID NO: 10, support for which can be found in the sequence listing and on page 5, line 28 of the specification. Claims 37, 41, 42 and 46 are amended to indicate that the β_2m protein is *human* β_2m. Claim 46 is further amended to delete "cytokine." Claim 48 is amended to clarify that the modified β_2m binds Class I MHC molecules with higher affinity than wild-type β_2m. Support for this amendment can be found, for example, on page 5, lines 3-8 of the specification.

The specification is amended to update the status of U.S. Serial No. 09/719,243, which issued as U.S. Patent No. 6,682,741.

Applicants expressly reserve the right to pursue protection of any or all of the canceled subject matter in one or more continuing applications. No new matter has been introduced by these amendments.

RESTRICTION/ELECTION

The requirement for restriction has been made final. However, Applicants note that Group I, the elected group, is related to Groups III, V and VI as product and process of use. Accordingly, upon allowance of Group I claim(s) (claims 37-39, 46-56 and 65-72), withdrawn process claims (claims 40-45, 61 and 62) that depend from, or otherwise incorporate all limitations of the allowed claim(s), are subject to rejoinder. In regard to the species election, Applicants elected mutant β_2-microglobulin fusion protein and B7.2 molecules. Upon allowance of a generic claim, Applicants are entitled to consideration of claims to additional species.

DOUBLE PATENTING REJECTIONS

Claims 46, 48, 49 and 52-56 are rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,682,741. Submitted herewith is a terminal disclaimer that disclaims the terminal portion of any patent granted in this application that would extend beyond the expiration date of U.S. Patent No. 6,682,741. Applicants submit that the filing of the terminal disclaimer obviates this rejection.

Claims 37-39 and 65 are rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,682,741 in view of Chada *et al.* (WO 97/24446). Applicants traverse this rejection. As discussed below in response to the rejection under 35 U.S.C. §102(b), Chada *et al.* do not teach a composition comprising a *peptide* antigen. Thus, Applicants submit claims 37-39 and 65 would not have been *prima facie* obvious in view of Chada *et al.* However, a terminal disclaimer is submitted with the current Amendment and Response, rendering this double-patenting rejection moot.

REJECTIONS UNDER 35 U.S.C. § 112, first paragraph

Claims 37-39, 48 and 65 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. The Office indicates this is a new matter rejection.

Claim 48 is rejected as lacking support for the full scope of the claim. Specifically, the Office alleges there is no support for a modified β_2 microglobulin that binds Class I MHC with the same or lower affinity than wild-type β_2 microglobulin. Claim 48 is amended herein to state that the modified β_2 microglobulin binds Class I MHC with higher affinity than wild-type β_2 microglobulin, rendering the rejection moot.

Claim 37 is rejected as allegedly being broader in scope than the disclosure since the claim is directed to a "composition" rather than a "vaccine composition." Applicants traverse this rejection. There is more than adequate written description for the compositions recited in claims 37-39 and 65. For example, on page 1, lines 6-7, the specification states that the disclosure "relates to *compositions* based on β_2 microglobulin, and the use of such *compositions* in immunological methods pertaining to the targeting of proteins to cell surfaces" (emphasis added). The specification further states on page 3, lines 14-15, "the invention also provides *compositions* and methods based on β_2m that are broadly applicable to achieve expression of any

desired target protein on the surface of a mammalian cell" (emphasis added). Thus, contrary to the Office's assertion, the specification is not restricted to vaccine compositions, but rather broadly describes β_2 microglobulin compositions for expression of proteins on a cell surface. Accordingly, Applicants request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Claims 37-39, 46-49, 52-56 and 65 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. The Office indicates that because the term "hβ2m S55V" includes human β_2 microglobulin proteins comprising any additional mutations, the description is not commensurate in scope with the claims. Furthermore, the Office alleges that if the term "β_2 microglobulin" is not restricted to human β_2 microglobulin, then it encompasses β_2 microglobulin from any number of mammalian species, the sequences of which may not be known. Although Applicants disagree with the Office's conclusion, solely in an effort to advance prosecution, claims 37, 38, 41, 45 and 49 are amended herein to reference SEQ ID NO: 10 as the sequence of hβ2m S55V. In addition, claims 37, 41, 42 and 46 are amended to specify that the fusion protein comprises *human* β2m. Therefore, Applicants submit rejected claims 37-39, 46-49, 52-56 and 65 (and all withdrawn claims) are supported by the written description. Accordingly, withdrawal of this rejection under 35 U.S.C. § 112, first paragraph is requested.

REJECTIONS UNDER 35 U.S.C. §102

Claims 37, 46, 52, 53 and 55 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Mottez *et al.* (*J. Exp. Med. 181*:493-502, 1995). The Office alleges Mottez *et al.* disclose a composition comprising a β_2 microglobulin fusion protein and an antigen (Cw3). The Office further states that Cw3 functions as a cell adhesion molecule because it mediates binding to cells with the appropriate T-cell receptors. Applicants traverse this rejection.

In order to anticipate a claim, a reference must teach each and every element of the claim. Claim 37 is directed to a composition comprising at least two individual components, an antigen and either (a) hβ2m S55V (SEQ ID NO: 10) or (b) a human β_2m fusion protein. In contrast, Mottez *et al.* describe a fusion protein in which the antigen (Cw3) is fused to mouse β_2

microglobulin and α3 of a mouse MHC molecule. Mottez *et al.* do not teach a composition comprising (1) an antigen *and* (2) a $h\beta_2m$ protein as claimed herein. Furthermore, the reference also does not teach human β_2 microglobulin or modified β_2 microglobulin (SEQ ID NO: 10).

In regard to claim 46, and dependent claims 52, 53 and 55, Mottez *et al.* do not teach a cell adhesion molecule as alleged by the Office. It was well known in the art as of the priority date of the instant application that "cell adhesion molecule" refers to a type of protein located on the cell surface that mediates binding to other cells or with the extracellular matrix. For example, U.S. Patent No. 5,514,788,[1] issued May 7, 1996, describes cell adhesion molecules as mediating "adhesion of white blood cells to vascular endothelium and other cell types" and teaches that cell adhesion molecules are "located on the plasma membrane of both white blood cells and vascular endothelium" and "interaction between adhesion molecules is similar to classical receptor ligand interactions with the exception that the ligand is fixed to the surface of a cell instead of being soluble." U.S. Patent No. 5,514,788 further teaches that cell adhesion molecules include such molecules as ICAM-1, ICAM-2, ELAM-1, VCAM-1 and LFA-1. Similarly, the instant specification indicates cell adhesion molecules include, for example, ICAM-1 and ICAM-2 (see page 3, lines 18-23). Thus, cell adhesion molecules do not include small antigenic peptides, such as Cw3 described by Mottez *et al.* One of ordinary skill in the art would recognize Cw3 as an antigenic peptide, which when bound to a MHC molecule, can be recognized by a specific T-cell receptor and contributes to activation of the T cell, not adhesion to the T cell. Furthermore, as stated above, Mottez *et al.* do not teach *human* β_2 microglobulin as claimed herein.

Therefore, since Mottez *et al.* do not teach each and every element of the pending claims, the claims are not anticipated. Accordingly, Applicants request withdrawal of this rejection under 35 U.S.C. §102(b).

Claims 37, 39, 46, 48, 52 and 53 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Chada *et al.* (WO 97/24446). The Office alleges Chada *et al.* teach β_2 microglobulin/cytokine fusion proteins (such as a β_2 microglobulin/EPO fusion protein) and a

[1] A copy of U.S. Patent No. 5,514,788 can be provided upon request by the Examiner.

composition comprising the fusion protein and a gene delivery vehicle, including viral gene delivery systems comprising viral antigen. Applicants traverse this rejection.

First, Applicants submit Chada *et al.* cannot be considered as a reference under 35 U.S.C. §102(b) since it was not published more than one year prior to the priority date of the instant application. Applicants note that the Office indicates the claims are not entitled to priority to the parent applications because they lack written description. However, as a divisional application, the specification of the current application is identical to parent Application Serial No. 09/719,243 (issued as U.S. Patent No. 6,682,741), which is identical to the specification of the parent PCT (PCT/US99/12309; published as WO 99/64597). Thus, the written description of the current application is identical to both of these prior applications. In addition, only minor differences exist between the parent provisional application (U.S. Provisional Patent Application Serial No. 60/088,813) and the current application, none of which relate to the written description provided for the claimed compositions. Therefore, the claims are entitled to priority to each of the parent applications, resulting in a priority date of June 10, 1998. Chada *et al.* was published July 10, 1997, less than one year before the priority date of the instant application.

Second, Chada *et al.* do not teach each and every element of the pending claims. As recited herein, claims 37-39 are directed to compositions comprising a peptide antigen and either (a) a hβ2m S55V protein (SEQ ID NO: 10) or (b) a human β2m fusion protein. Although Chada *et al.* teach that fusion proteins can be delivered using a viral gene delivery system, the reference does not teach administration of the fusion protein with an antigen, particularly a peptide antigen as claimed herein. The specification teaches that peptide antigens are antigens that bind to MHC molecules (see, for example, page 15, lines 4-14 and page 22, line 29 to page 23, line 15); therefore, Chada *et al.* do not teach compositions comprising a β2m protein and a peptide antigen. Accordingly, Applicants request withdrawal of this rejection under 35 U.S.C. §102(b).

Claims 37-39, 46, 48, 49, 52-56 and 65 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Ribaudo *et al.* (WO 99/64597). Ribaudo *et al.* is a prior filed application to which the instant application claims priority. As discussed above, the instant application is entitled to claim priority to Ribaudo *et al.* (WO 99/64597), therefore it is not a valid prior art reference. Thus, Applicants request withdrawal of this rejection under 35 U.S.C. §102(b).

CLAIM OBJECTION

Claims 48 and 49 are objected to because claim 48 recites "class 1" rather than "class I." Claim 48 is amended accordingly, rendering the objection moot.

CONCLUSION

It is respectfully submitted that the present claims are in a condition for allowance. Should the Examiner have further questions or comments with respect to examination of this case, it is respectfully requested that the Examiner telephone the undersigned so that further examination of this application can be expedited.

Respectfully submitted,

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